REMARKS

This is responsive to the Final Office Action mailed December 31, 2003.

Rejections Under 35 U.S.C. 103

The Examiner maintained the rejection of claims 1-12 under 35 U.S.C. § 103 as unpatentable over US patent 4,740,374 or US patent 5,866,157, individually or combined with US patent 5,271,946. Applicant respectfully requests reconsideration.

As an initial matter, Applicant notes that the Examiner has stated in the Office Action on page 2, last paragraph, that the '374 and the '157 patents "do not disclose the organic acid in the powder form or the mean diameter of the powder particles." The Examiner relies exclusively on the teaching of sodium acetate having a particle size of 0.1-200 micrometers found in the '946 patent. Therefore, Applicant respectfully requests that the rejection of the claims as based on the '374 patent or the '157 patent individually be withdrawn because these patents do not provide the elements of the claimed invention and motivation to modify the teachings contained therein in such a way that one of ordinary skill in the art would have a reasonable expectation of success in obtaining the claimed invention.

The Examiner suggests that "it is within the skill in the art to determine the diameter of the particle in order to achieve a beneficial effect." Office Action at page 4. In support of this contention, the Examiner notes that the "references are silent regarding the state of sodium acetate, and that does not exclude its presence as a powder." While this statement is formally true, it nevertheless does not follow that one of ordinary skill in the art would be motivated to use sodium acetate in powder form, particularly with particles of a defined size as claimed by Applicant. Applicant first found that the skin permeability of the salt form of the base drug can be improved by means of the ion-pair formed by a particular particle size of the organic acid salt as described on page 4, lines 9-19. There is simply nothing in either of the primary references that would suggest the particle range for an ion-pair formation to the person skilled in the art. A lack of disclosure in a reference about a property (i.e., particle size) does not suggest anything at all to the skilled artisan, and certainly does not provide the motivation required under the law.

The Examiner relies on the '946 patent to supply the particle size range for sodium acetate. However, the size range disclosed in the '946 patent (0.1-200 μm) is not that claimed by Applicant (0.1-100 μm), although it does include Applicant's claimed range.

The Examiner acknowledged the teaching of Applicant's specification with respect to particle sizes of 0.1-10 μm. Office Action at page 4. Certain other statements made by the Examiner regarding the teachings of the specification are erroneous, however.

The Examiner stated that "applicant did not show the effect of particle size outside the claimed range, i.e., below 0.1 and above 100." This is incorrect, because Applicant presented additional data in the specification for particle sizes between 10 and 100 μm. The following Examples show the effect of 10-100 μm particle sizes: Example 2 (43 μm), Example 3 (91 μm), Example 4 (43 μm), Example 5 (43 μm), Example 7 (43 μm), Example 8 (91 μm), Example 10 (91 μm), Example 12 (43 μm), Example 13 (91 μm), Example 14 (50 μm or smaller), and Example 15 (100 μm or smaller). Thus, contrary to the Examiner's assertion, Applicant clearly taught the effects of particles sizes across the whole claimed range. Moreover, Applicant's specification also provided information for particle sizes outside of the claimed range (see below).

The Examiner stated that "the comparative examples of record used the ungrounded sodium acetate, i.e., the crystals and not the powder." This statement is does not correctly reflect Applicant's disclosure. In the specification, sodium acetate is selected by its particle size irrespective of whether or not it is crystals. In the comparative examples, Applicant used <u>both</u> ungrounded and grounded sodium acetate to show the effects of particle size greater than 100 μm. Comparative Examples 4 and 8 used ground organic acid salts having particle sizes of 200 μm and 139 μm, respectively. This data is shown in Fig. 2 (200 μm particles) and Fig. 3 (139 μm particles). The other comparative examples used particles of 535 μm.

Therefore, Applicant has demonstrated that particle sizes of 0.1-100 μm have superior properties for the claimed compositions as compared to particles of >100 μm.

As noted above, the Examiner stated on page 4 of the Office Action that "it is within the skill in the art to determine the diameter of the particle in order to achieve a beneficial effect." The Examiner indicates that the '374 and '157 patents teach the presence of sodium acetate for improved percutaneous absorption and that the '946 patent, having taught a percutaneous preparation, supplies the motivation to select the claimed particle size. Applicant respectfully disagrees, because none of the cited patents provide any motivation to one of ordinary skill in the art to select and use the particle sizes claimed by Applicant.

Regarding the Examiner's statement that it would have been obvious to one of ordinary skill in the art to "select the particle size of the powder that [is] required to achieve the desired rate of permeation across the skin," (Office Action page 5) Applicant respectfully disagrees. Based on the teachings of the '946 patent (0.1-200 μm), one of ordinary skill in the art would not have expected that particles of less than 100 μm, i.e., 0.1-100 μm, would have the superior properties demonstrated by Applicant. This is particularly true when one considers that the purpose that the '946 patent teaches for sodium acetate particles is as a pore-forming agent for sustained release components (col. 2, lines 20-33), not for increasing percutaneous absorption via an ion-pair formation.

Thus one skilled in the art would not look to the '946 patent for the teaching at all as being directed to the use of sodium acetate for a completely different purpose. Alternatively, the skilled artisan would not be motivated to select the particular range claimed by Applicant because there is no motivation in the '946 patent to use particles in the claimed range as distinct from the full range disclosed in the application. Neither the '374 patent nor the '157 patent provide any information regarding the advantageous use of the claimed particle sizes, and therefore the '374 and '157 patents do not provide the motivation to use the claimed particle sizes that is lacking from the '946 patent. Accordingly, based on the disclosures of the '946, '374 and '157 patents, one of ordinary skill in the art would not have been motivated to select the

range of particle sized claimed by Applicant in order to make the claimed percutaneous absorption compositions.

CONCLUSION

In view of the foregoing remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this response, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

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